



## Breast Pathology in Adolescent Girls

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**Annotation:** In the structure of adolescent diseases (usually benign) breast cancer is 5-12%. Breast cancer is detected extremely rarely (no more than 1% of all cases of breast disease). The review contains current data on the most common focal pathology of the mammary glands in adolescent girls: focal hyperplasia, cysts and fibroepithelial tumors of the mammary glands. Clinical manifestations, morphological picture, diagnostic procedures are described. The main approaches to the treatment of patients with focal pathology of the mammary glands are determined. The presented information is necessary for the timely diagnosis of focal pathology of the mammary glands, the choice of examination tactics, treatment and necessary measures for the prevention of oncological diseases in children

**Key words:** adolescent mammology, breast diseases, juvenile papillomatosis, cyst, fibroadenoma, leaf-shaped tumor.

## INTRODUCTION

According to existing classifications, in childhood, anomalies and developmental disorders of the mammary glands, non-tumor diseases, as well as benign and malignant tumors are distinguished [1-3]. At the same time, the maximum risk of developing benign and malignant tumors of the mammary glands is typical for children aged 7 to 17 years [2, 4]. In the structure of children's diseases, deviations in the development or diseases of the mammary glands account for 5-12% [4]. At the same time, the frequency of oncological pathology does not exceed 1% [5, 6], and the most common variant is benign diseases [7, 8]. Among benign nodular diseases in adolescence, the most common are fibroadenomas, breast cysts, focal hyperplasia, intraductal papillomas.

### Focal hyperplasia of the mammary glands

In adolescence, focal hyperplasia is more often noted after 15 years [12]. There are no specific clinical manifestations for different types of hyperplasia. There may be complaints of soreness of the mammary glands, discomfort, especially before menstruation, as well as discharge from the nipple (transparent, white type of colostrum). As a rule, this is a palpable induration with a negative Koenig's symptom, when, when the position of the patient's body changes (from vertical to horizontal), the previously palpable induration "dissolves" in diffusely indurated mammary gland tissues [12, 13].

The most informative diagnostic option is an ultrasound examination (ultrasound), in which focal compaction of the glandular tissue or concomitant focal changes (cyst, papilloma) are visualized. The data of magnetic resonance imaging (MRI) are often nonspecific, a picture of an unchanged mammary gland is typical [14, 15]. Differential diagnosis is carried out with juvenile papillomatosis, adenosis, fibrocystic changes.

Morphologically, hyperplasia can be lobular or ductal. Histological changes in focal lobular proliferation are layers of white dense tissue of various widths with small cysts or granular inclusions [12, 13, 16].

The cause of such changes in girls is a dishormonal condition associated with progesterone deficiency. In this case, encouraging results can be achieved using conservative treatment. Locally apply progesterone in the form of a gel, 2.5 mg on the skin of the breast from the 16th to the 25th day or continuously. The standard cycle is 3 months, after which ultrasound control is performed to assess the effect achieved. The course can be prolonged up to 6 months in case of insufficient effectiveness or repeated with an interval of 1 month to consolidate the result [12].

### **Intraductal papilloma**

Juvenile papillomatosis ("Swiss cheese disease") is more often detected in girls [8, 12], the average age of onset of pathology is 19 years [9]. A family history of breast carcinoma was noted in 28% of cases [10], in 5% of patients subsequently malignant transformation is noted [10]. Clinically, intraductal papilloma manifests itself as a bumpy, localized mobile formation, resembling fibroadenoma in consistency [9, 13]. In this case, the main complaint is discharge from the nipple, usually bloody. However, if the process is located in the ducts of the second or third order, the excretions are more often dirty or may be absent altogether [12].

According to ultrasound data, intraductal growths are noted, often well supplied with blood (in the color Doppler mapping mode) [9, 14]. The extent and extent of the lesion is visualized by contrasting the ducts or by using endoscopic techniques.

Macroscopically (on a cut), intraductal papilloma is a collection of multiple cystic cavities located among fibrous tissue. Microscopic examination reveals proliferating papillary tissue on fibrovascular peduncles in many terminal ductal-lobular units [12, 13]. It must be differentiated primarily from intraductal cancer.

Surgical treatment - sectoral resection with urgent histological examination. Peripherally located papillomas are prone to recurrence [12].

### **Breast cyst**

Breast cyst is the most common pathological formation of the mammary gland in women of reproductive age (in 20-50%) with a maximum frequency in the perimenopausal period, but can be detected at any age [8, 12, 13]. The size of the formation is variable in the menstrual cycle, with a maximum in the premenstrual period. Clinical symptoms are polar - from the absence of any changes with small sizes and "unfilled" cysts to palpable formation with large sizes and superficial localization. Palpation characteristics of cysts: rounded contour, elastic consistency, mobility in the surrounding tissues [15].

Ultrasound is the best method for diagnosing cysts. A well-defined, anechoic formation of a round or oval shape is visualized, with the effect of posterior shading (Fig. 1). Sometimes the cyst may be hypoechoic (complicated cyst) or heterogeneous in structure in the presence of intracystic contents. Usually there is refraction of the lateral edges. For differentiation with a solid formation, pressure with a transducer on the cyst (it "falls off") or the elastography mode can be used. To

differentiate intracystic formations, color Doppler mapping is used [14, 15]. MRI may be an option, in which the usual characteristics are: T1 without contrast - smooth contour, low signal intensity; T1 with contrast - no enhancement; T2 - smooth contour, extremely high, homogeneous signal intensity. When visualizing large cysts (> 2 cm), as well as in cases of complicated cysts, aspiration biopsy with cytological examination is indicated [13, 14]. Differential diagnosis is carried out with fibroadenoma, leaf-shaped tumor, galactoceles. Papillary growths in the cyst should be differentiated from intracystic cancer.

Conservative treatment is indicated for multiple small cysts, which is usually interpreted as "mastopathy with a predominant cystic component." To correct such changes, a wide range of so-called basic therapy is used, including phyto- and vitamin therapy, the appointment of immunocorrectors and adaptogens [12]. In cases of combined pathology (hormonal imbalance), correction is carried out using hormonal preparations - local (progesterone in the form of a gel) or systemic, prescribed by a gynecologist if there are appropriate indications, for example, in case of hyperplastic and inflammatory gynecological diseases. In the case of effective treatment, a dynamic examination shows a reduction in most of the existing formations.

Surgical treatment (sectoral resection with urgent histological examination) is indicated for large (> 2 cm), actively accumulating cysts, or in cases of failure of conservative or sclerosing therapy, or when obtaining a doubtful cytological conclusion [13]. The prognosis is favorable, since malignant transformation of simple cysts does not occur, and the probability of malignancy of a complex cyst does not exceed 0.3% [12].

### **Fibroadenoma of the breast**

Fibroadenomas of the mammary glands are the most common variant of connective tissue-epithelial tumors and account for up to 20% of all pathological formations of the mammary gland [4, 13, 16]. Usually these are single formations, but in 15% of cases there is a multiple nature of the lesion [17]. Fibroadenomas of the mammary glands are found in all age groups, but most often at the age of up to 20-35 years [2, 16, 17].

Clinically, fibroadenoma is a dense, elastic, mobile formation ranging in size from a few millimeters to 3-4 cm (and up to 20 cm with a giant tumor). There may be a positive symptom of Koenig (in the supine position).

Ultrasound reveals an oval, round or lobular mass, homogeneous, of low intensity, with internal echogenicity, which may be heterogeneous (Fig. 2). A thin echogenic rim and pronounced posterior acoustic enhancement are often noted. Atypical for fibroadenoma will be uneven microlobular edges, posterior acoustic shadow, active vascularization, visualized in color Doppler mapping. In such situations, a cytological or histological biopsy is always indicated [11, 14]. On MRI, an oval-shaped formation with smooth or lobulated borders is encountered, with a variable pattern of enhancement [14].

Morphologically, depending on the nature of growth, intra-, pericanicular and mixed forms of fibroadenomas are distinguished. Macroscopically, fibroadenomas are grayish in color, lobed in structure. The tumor is clearly delimited from the surrounding tissues, and the severity of stromal fibrosis determines its consistency. Histologically, this is a two-component formation, represented by both epithelial and connective tissue structures [17].

Differential diagnosis is carried out with any volumetric neoplasm of the mammary gland - both benign and malignant.

The management of patients with fibroadenomas (especially in the case of multiple fibroadenomas) includes both dynamic observation and active intervention up to sectoral resection with urgent histological examination or tumor enucleation.

The main indications for surgical treatment are [13]:

- large sizes of education (> 2 cm);
- tumor vascularization (according to color Doppler mapping);
- fast growth;
- the desire of the patient to get rid of the "bumps" in the mammary gland.

In all other cases, dynamic monitoring may be recommended. The latter is also due to the fact that malignant transformation of fibroadenomas is rare [12, 17]. The prognosis is generally favorable.

### Leaf tumor

A rare group of tumors that make up no more than 0.3% of all neoplasms of the mammary glands [18]. In adolescents, it occurs in 0.4% of cases of benign tumors [8, 9, 18].

From clinical and morphological positions, 3 main variants of leaf-shaped tumors are distinguished [18]:

- simple (benign) leaf-shaped tumor (40-80%);
- borderline (intermediate) leaf-shaped tumor (10-20%);
- malignant leaf-shaped tumor (5-30%).

The characteristic clinical symptoms of a leaf-shaped tumor usually include the presence of a dense mobile mass ranging in size from 5 to 22 cm, which is sometimes closely associated with breast tissue and can quickly increase in size. In some cases, a well-developed network of subcutaneous venous vessels is determined. The skin over the lesion may become thinner and ulcerate, and serous discharge from the nipple is often noted (Fig. 3) [17, 19]. For leaf-shaped tumors, a two-phase clinical course is characteristic, in which the "phase of relative rest" is replaced by a stage of rapid growth.

With ultrasound, an oval formation with a clear, even contour is visualized (with a large volume of the tumor, a convex probe is used). In this case, cystic inclusions are often noted - leaf-shaped tumors are more heterogeneous than ordinary fibroadenomas. It is believed that heterogeneity correlates with an increase in malignant potential [9, 14, 15]. To determine the nature of the tumor blood supply, it is necessary to use the color Doppler mapping mode, which is important for differential diagnosis [5, 15, 19]. When conducting MRI, the results are not always specific: on T-1 and T2-modes without contrast - non-specific, large, lobulated, space-occupying formation; on T-1 with contrast - lobular volumetric education without washing out the contrast.

The cytological method in the diagnosis of a leaf-shaped tumor is informative only in 30% of cases [13, 18]. This is due to the difficulties of morphological interpretation due to the variability of the structure of the tumor. The most common diagnosis is breast cancer. Morphologically, leaf-shaped tumors have a lobed, leaf-like structure. In the malignant variant, the loss of the leaf-like structure is characteristic with the appearance of tissue fields of varying degrees of density (similar to "fish meat" sarcoma). There may be areas of cartilage and bone density.

For the differential diagnosis of a leaf-shaped tumor from fibroadenoma and breast sarcoma, in the practice of "adult" mammologists, a radionuclide study with <sup>99m</sup>Tc is used. In a malignant leaf-shaped tumor, the accumulation of the radiopharmaceutical is determined on early and late images,

and in a benign tumor, only in the early ones [18]. If breast cancer is suspected, for the purpose of verification, it is necessary to perform a core biopsy with a histological examination of the material [13, 18, 19].

Therapeutic tactics is based on the obtained diagnostic and morphological information [18, 20]. With a benign leaf-shaped tumor and its small size, sectoral resection is indicated with urgent histological control of the resection margins. In the case of a large tumor deforming the mammary gland, mastectomy without lymphadenectomy with mammoplasty is indicated [18-20]. Tumor enucleation, even at small sizes, is unacceptable due to the high risk of recurrence, regardless of the histological variant of the tumor [17]. The prognosis of leaf-shaped tumors is as follows [18, 19]:

- benign leaf-shaped tumors are not prone to recurrence (<10% in 10 years);
- relapses tend to be more malignant;
- intermediate variant recurs in 29%, malignant — in 36% of cases;
- possible metastasis to the lungs (malignant leaf-shaped tumor);
- five-year survival rate for malignant variant is 55-75%.

### **Mammary cancer**

Oncological pathology of the mammary glands in children is extremely rare. In most cases, this is the so-called juvenile or secretory cancer, which, according to some data, accounts for 0.046% of all malignant tumors [5]. Juvenile cancer is more often detected in patients over the age of 12 [6, 12], although a case of the disease has also been described at the age of three [12].

Clinically, breast cancer is usually represented by a tumor formation with a clear contour, small in size, although in the older age group (young women of the reproductive period), the size can be significant - up to 12 cm [21]. Separate observations are described when the disease proceeded as a diffuse form with symptoms of mastitis-like cancer [22].

On macroscopic examination, a well-defined tumor node is determined. The microscopic picture is quite characteristic and is represented by glandular and solid structures consisting of large cells with a well-defined vacuolated cytoplasm. A significant part of the cells has an optically empty cytoplasm ("hypernephroid" type). The lumens of the glandular structures are filled with eosinophilic PAS-positive secretion. Often, the central part of the tumor node is represented by a hyalinized stroma without cancer cells. Tumor cells in this form of cancer usually express epithelial membrane antigen,  $\alpha$ -lactoglobulin, and B-100 protein [22]. Secretory cancer usually has a high degree of differentiation and negative expression of estrogen receptors [22].

The prognosis for juvenile cancer is relatively favorable, with a long (> 5-10 years) relapse-free interval [1, 5]. Long-term progression is also rarely detected, and lethal cases in childhood have not been described [22]. However, with increasing age of patients, the prognosis of the disease worsens.

### **Conclusion**

It must be remembered that histogenetically different tumors of the mammary glands can occur in children. This is a small cohort of patients, no more than 5-12% with benign diseases and less than 1% with malignant pathology. In this regard, it is important to inform pediatricians about the options for focal pathology of the mammary glands in children, the need for their timely diagnosis and specialized treatment.



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